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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,404	06/21/2006	Jonathan S. Stamler	24862-516N01US	1777

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EXAMINER	
SAUCIER, SANDRA E	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
07/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,404	STAMLER ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 4-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/9/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 are pending. Claim 3 is considered on the merits. Claims 1, 2, 4-6 are withdrawn from consideration as being drawn to a non-elected invention.

Election/Restriction

Claims 1, 2, 4-6 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made without traverse in Paper No. 5/26/09.

Specification

The disclosure is objected to because of the following informalities: Examples are either prophetic or have actually been performed. If prophetic, the tense of the verbs should be in the present. If actually performed, the tense of the verbs should be in the past. The tense of the verbs in the examples switch from past tense to present tense, see Example II. Therefore, it is uncertain whether some of these examples are prophetic or have actually been carried out on a human patient. Appropriate correction and clarification is required.

Claim Objections

Claim 3 is objected to because of the following informalities: Please insert "a hemoglobin-containing" blood substitute in the second line of claim 3 for clarity. It is noted that in the specification on page 4, the definition for blood substitute is presented which states that the blood substitute contains hemoglobin. As not all blood substitutes known in the art contain hemoglobin, it is requested that the claim incorporate this language in order to promote ease of reading and interpretation.

Claim Rejections - 35 USC § 112

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim uses the word "co-infusing", and defines co-infusion to mean contemporaneously or shortly before or shortly after another on page 4. However, the term "shortly" is not defined, so the length of time which co-infusing could be interpreted to be separately at a different time is not definite. Further, it is uncertain whether the term encompasses a mixing of the components, i.e. red cells or hemoglobin containing red cell substitute and nitrite, in one container, left for a period of time and then infused, or if they must be in separate containers. The metes and bounds of the method claim are not clear.

ENABLEMENT

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of an inorganic nitrite with a red cell substitute containing hemoglobin, does not reasonably provide enablement for the use of erythrocytes and inorganic nitrite. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification generically teaches that red cell transfusions lead to increased morbidity or mortality as a reason for performing the claim procedure, i.e. concomitant infusion of red cells and nitrite. However, while the vasoconstrictive response to the infusion of hemoglobin-containing acellular substitutes is well known, the infusion of red cells does not appear to have increased morbidity or mortality or even vasoconstrictive effects. Nelle *et al.* [U] teach that mean arterial blood pressure did not change after red cell transfusion and that neither vasoconstriction nor vasodilation occurred with transfusion (abstract). Carson *et al.* [V] teach that blood transfusion does not appear to influence the risk of 30 or 90 day mortality in an elderly population undergoing surgical repair for hip fracture (abstract). Engoren *et al.* [W] teach that red cell transfusion decrease mortality in intensive care patients (abstract). Thus, the medical literature teaches that transfusion of erythrocytes does not lead to increased mortality in patients, which is the specific medical reason given for the concomitant administration of red cells and nitrite (page 2).

Example III is prophetic, and is the only example drawn to "co-infusion", nitrite and red cells are not infused at the same time, but rather first infusion of nitrite, then infusion of red cells. No benefit is clearly shown nor is a benefit apparent from the state of the art for the separate, but concomitant (co-infusion) administration of red cells and nitrite in terms of the stated reasons for such a performance of the claimed method, which are reduced mortality and morbidity due to red cell transfusion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action: (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/30006 [N].

The claim is directed to a method of treating a patient comprising co-infusing the blood substitute or red blood cells and an inorganic nitrite at the rate of 0.01 to 10 micromoles per minute.

WO 96/30006 discloses problems with the infusion of blood substitutes containing hemoglobin which causes vasoconstriction due to the scavenging of nitric oxide (page 1-2). Thus, the reference discloses methods to overcome this problem. A composition comprising nitrosylated hemoglobin is specifically mentioned (page 4).

Also, on page 5 another method for inhibiting the vasoconstrictive and nitric oxide depleting effects of hemoglobin and heme-containing based blood substitute composition by the concurrent systemic administration of nitric oxide or a compound which donates, releases or transfers nitric oxide. Such administration can, for example, be by inhalation or intravenously, separately or in composition with the blood substitute.

A compound which donates nitric oxide (nitrosylation) is sodium nitrite (page 10). The term "nitrosylation" refers to the addition of NO to a thiol group, oxygen, carbon or nitrogen by chemical means (page 24).

Therefore, the reference generically teaches the concurrent administration of a hemoglobin-containing blood substitute and sodium nitrite. The reference also teaches the nitrosylation of proteins *in vivo*, as a therapeutic modality (page 13). Therefore, the concurrent administration of an NO donating compound, such as sodium nitrite and a hemoglobin-containing blood substitute is again taught. The reference lacks the concentration of nitrite to be administered. However, in Example 19, it is taught that equimolar quantities of sodium nitrite and hemoglobin should be reacted. Therefore, the quantity of sodium nitrite and the rate of administration of sodium nitrite can be calculated from the quantity of hemoglobin to be administered. That the values are not in the same units as claimed is of little patentable weight in the absence of evidence to the contrary.

Also, with regard to the differences in concentrations or dosage between the instant claims and the disclosure of the prior art, see MPEP 2144.05 I. and II.

Generally differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation, *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955 (CCPA 1960). MPEP 716.02(d).

One of ordinary skill in the art would have been motivated at the time of invention to perform this method in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Conclusion

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). It is applicants' burden to indicate how amendments are supported by the ORIGINAL disclosure. Due to the procedure outlined in MPEP 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 USC 102 or 35 USC 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is (571) 272-0922. The examiner can normally be reached on Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, M. Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sandra Saucier/
Primary Examiner
Art Unit 1651